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Intraoperative Driving Pressure–Guided High PEEP vs Standard Low PEEP for Postoperative Pulmonary Complications

Writing and Steering Committees for the DESIGNATION–Investigators

IMPORTANCE The effect of individualized high positive end-expiratory pressure (PEEP) and recruitment maneuvers, targeting a low driving pressure, on clinical outcomes in patients undergoing open abdominal surgery is uncertain.

OBJECTIVE To compare driving pressure–guided high PEEP and recruitment maneuvers with standard low PEEP without recruitment maneuvers with respect to postoperative pulmonary complications.

DESIGN, SETTING, AND PARTICIPANTS Randomized clinical trial of 1435 adults at increased risk for postoperative pulmonary complications who were scheduled for open abdominal surgery. The trial was conducted at 29 sites in 5 countries across Europe from April 2019 to December 2024; final follow-up was in March 2025. Statistical analysis was conducted in May 2025.

INTERVENTION Patients were randomized to undergo intraoperative ventilation with driving pressure–guided high PEEP and recruitment maneuvers (n = 718) or to intraoperative ventilation with standard low PEEP (n = 717). All patients received low tidal volume ventilation.

MAIN OUTCOMES AND MEASURES The primary outcome was a composite of pulmonary complications within the first 5 postoperative days, including severe respiratory failure, bronchospasm, suspected pulmonary infection, pulmonary infiltrates, aspiration pneumonitis, atelectasis, acute respiratory distress syndrome, pleural effusion, cardiopulmonary edema, and pneumothorax. Among the 16 prespecified secondary outcomes, 4 concerned intraoperative complications, including hypotension (decrease in mean arterial pressure of >20% for >3 minutes) and desaturation (Spo_2 <92% for >1 minute).

RESULTS Among 1468 adults, 1435 (98%) completed the trial (median [IQR] age, 66 [57-74] years; 52% female). In the primary analysis population, the primary outcome occurred in 142 of 718 patients (19.8%) in the driving pressure–guided high PEEP group compared with 125 of 717 patients (17.4%) in the low PEEP group (absolute difference, 2.5% [95% CI, −1.5% to 6.4%]; *P* = .23). The incidence of hypotension (382 [54.0%] vs 317 [45.0%]) and use of vasoactive agents (224 [32.0%] vs 130 [18.8%]) was higher in the high PEEP group; the incidence of intraoperative desaturation (6 [0.8%] vs 20 [2.8%]) was higher in the low PEEP group.

CONCLUSIONS AND RELEVANCE Among patients at increased risk for postoperative pulmonary complications undergoing open abdominal surgery under general anesthesia, intraoperative ventilation with driving pressure–guided high PEEP and recruitment maneuvers, compared with a strategy with standard low PEEP, did not reduce postoperative pulmonary complications.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT03884543

Visual Abstract
Research Summary
Supplemental content

Group Information: The members of the Writing and Steering Committees for the DESIGNATION–Investigators appear at the end of the article. The members of the DESIGNATION–Investigators are listed in Supplement 5.

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JAMA. doi:10.1001/jama.2025.23373
Published online December 3, 2025.

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Postoperative pulmonary complications are common after major surgery[1] and are strongly associated with morbidity, mortality,[2-4] and health care costs.[5,6] Patients undergoing open abdominal procedures are particularly vulnerable, with risk stratification tools identifying this population at increased risk.[3,7] It is estimated that 55 million abdominal surgeries are performed annually worldwide.[8] Even modest reductions in the incidence of postoperative pulmonary complications could lead to meaningful improvements in patient outcomes and considerable reductions in health care expenditures.

Intraoperative lung-protective ventilation aims to reduce postoperative pulmonary complications by using low tidal volumes, moderate to high levels of positive end-expiratory pressure (PEEP), and recruitment maneuvers.[9] One randomized clinical trial showed fewer pulmonary and extrapulmonary complications with this combined approach compared with high tidal volumes without PEEP.[10] However, later trials isolating PEEP—while maintaining low tidal volumes—showed no clear benefit.[11,12] Driving pressure, a marker of lung strain, is independently associated with postoperative pulmonary complications.[13] When PEEP improves aeration, driving pressure may decrease; if it causes overdistension, driving pressure may increase.[14] It has therefore been proposed to individualize PEEP during surgery.[15] Two recent trials evaluated individualized PEEP strategies,[16,17] but complex designs, including postoperative care or bundled interventions, limit conclusions about intraoperative PEEP titration alone.

The Driving Pressure During General Anesthesia for Open Abdominal Surgery (DESIGNATION) trial was conducted to test whether an intraoperative ventilation strategy with an individualized, driving pressure-guided, high level of PEEP and recruitment maneuvers reduced the incidence of postoperative pulmonary complications during the initial 5 postoperative days compared with an intraoperative ventilation strategy with standard low PEEP without recruitment maneuvers in patients who are at increased risk for these complications and are undergoing open abdominal surgery.

Key Points

Question Do intraoperative driving pressure–guided high positive end-expiratory pressure (PEEP) and recruitment maneuvers decrease postoperative pulmonary complications in patients undergoing open abdominal surgery compared with standard low PEEP without recruitment maneuvers?

Findings In this randomized clinical trial of 1435 adult patients undergoing open abdominal surgery under general anesthesia, the rate of postoperative pulmonary complications was 19.8% among those randomized to undergo driving pressure–guided high PEEP compared with 17.4% among those randomized to undergo standard low PEEP; the difference was not statistically significant.

Meaning An intraoperative ventilation strategy targeting the lowest driving pressure through individualized PEEP and recruitment maneuvers did not reduce postoperative pulmonary complications in patients undergoing open abdominal surgery.

Methods

Study Design and Oversight

This was an international, investigator-initiated, assessor-blinded randomized clinical trial. The study protocol was previously published,[18] designed in collaboration with patient representatives, and is available in Supplement 1. Amendments to the study protocol are provided in Supplement 2, and the final statistical analysis plan, written prior to locking the database, is provided in Supplement 3. The study was registered at ClinicalTrials.gov (NCT03884543). The study was approved by the institutional review board of Amsterdam University Medical Centers, Academic Medical Center location. Written informed consent was obtained from all participants. An independent data and safety monitoring board oversaw the conduct of the study and reviewed blinded safety data. On-site monitoring was performed to ensure adherence to the protocol and completeness of data. The trial was conducted and reported according to the Consolidated Standards of Reporting Trials (CONSORT) guidelines.[19]

Patients

Patients were eligible for inclusion if they were 18 years or older, were scheduled for open abdominal surgery under general anesthesia, and had an intermediate or high risk of developing postoperative pulmonary complications according to an Assess Respiratory Risk in Surgical Patients in Catalonia (ARISCAT) score of 26 or higher.[7]

Patients were excluded if they were scheduled for laparoscopic or robotic surgery, open abdominal surgery combined with intrathoracic procedures, or surgery requiring prone or lateral positioning. Additional exclusion criteria included body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) higher than 40, confirmed pregnancy, participation in another interventional study under general anesthesia, and not having sufficient reflection time before giving informed consent (defined as <12 hours between consent discussion and surgery). Patients were also excluded if they had received ventilation for more than 30 minutes within the last 30 days preceding surgery; were expected to require postoperative ventilation in the intensive care unit (ICU) or postanesthesia care unit; had persistent hemodynamic instability or intractable shock; or had severe cardiac disease, defined as New York Heart Association (NYHA) class III or IV, acute coronary syndrome, or persistent ventricular tachyarrhythmias. Other exclusion criteria included prior major lung surgery (eg, lung resection), a history of acute respiratory distress syndrome, severe chronic obstructive pulmonary disease (GOLD stage III/IV or requiring home oxygen or noninvasive/invasive home ventilation), or absence of written informed consent.

Randomization and Interventions

Eligible patients were randomized in a 1:1 ratio to undergo an intraoperative ventilation strategy with an individualized, driving pressure-guided, high level of PEEP and recruitment maneuvers (the high PEEP group) or an intraoperative ventilation strategy with standard low PEEP without recruitment

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maneuvers (the low PEEP group). A computer-generated allocation sequence using permuted random block sizes of a maximum of 8 and stratified per study site and BMI (≤30 vs >30) was used.

Patients randomized to the high PEEP group underwent a recruitment maneuver before and after the decremental PEEP trial, after any disconnection from the ventilator during the surgical procedure, and within 1 hour before extubation. Recruitment maneuvers were performed after assuring a stable hemodynamic situation, judged by the attending anesthesiologist. With each recruitment maneuver, and during the decremental PEEP trial, the ventilator remained in a volume-controlled ventilation mode, with the respiratory rate set at 15 breaths per minute. During the recruitment maneuver, PEEP was increased every 15 seconds from 5 cm H_2O up to 20 cm H_2O in steps of 5 cm H_2O. Then, PEEP was decreased every 20 seconds in steps of 2 cm H_2O until a minimum level of 6 cm H_2O. With every step, the resulting driving pressure was calculated by subtracting PEEP from the plateau pressure and plotted in the driving pressure–PEEP graph, mandated by the study protocol (Supplement 1). From this graph, the highest PEEP with the lowest driving pressure was identified. After a second recruitment maneuver, this PEEP level was used until tracheal extubation. If the graph did not display a minimum driving pressure, a PEEP level of 12 cm H_2O was to be used. All intraoperative trial interventions were performed manually by the attending anesthesiologist. A visual representation of the decremental PEEP trial and recruitment maneuvers is provided in eFigure 1 in Supplement 4; feasibility of the intervention was shown in a safety and feasibility study.[20] Patients randomized to the low PEEP group were ventilated with a PEEP level of 5 cm H_2O throughout surgery. They neither received recruitment maneuvers nor a decremental PEEP trial.

If there was any concern about the patient's safety or if the surgeon considered that the level of PEEP interfered with the surgical procedure, PEEP could be adjusted. Likewise, PEEP could also be adjusted for the following reasons: hypotension, defined as a decrease in mean arterial pressure of more than 20% compared with preoperative mean arterial pressure and lasting longer than 3 minutes; not responding to intravenous fluids or vasoactive drugs; new arrhythmias not responding to the treatment suggested by the Adult Advanced Cardiovascular Life Support guidelines[21]; need for vasoactive drugs at dosages higher than acceptable according to the discretion of the anesthesiologist in charge; need for massive transfusion, with more than 5 units of blood to maintain hematocrit greater than 21% (or hemoglobin >7 mg/dL); or life-threatening complications.

Standard perioperative care, including anesthesia, neuromuscular monitoring and reversal, pain management, physiotherapy, and fluid therapy, followed local protocols; adherence to Enhanced Recovery After Surgery (ERAS) guidelines was encouraged.[22]

Blinding

At every center, at least 2 investigators obtained patient data: one investigator was aware of the patient allocation and obtained intraoperative data, the other remained blinded to the intraoperative interventions and assessed outcomes. A separate intraoperative and postoperative data entry environment was created to ensure blinding of the outcome assessor.

Primary Outcome

The primary outcome was a composite of postoperative pulmonary complications and was defined as having occurred if any preselected complication developed within the first 5 postoperative days. The components of the composite included severe respiratory failure, bronchospasm, suspected pulmonary infection, new pulmonary infiltrates, aspiration pneumonitis, new atelectasis, acute respiratory distress syndrome, new pleural effusion, new cardiopulmonary edema, and new pneumothorax. Definitions for the components are described in the study protocol (Supplement 1).

Secondary Outcomes

The 16 secondary outcomes were mild respiratory failure, intraoperative complications (desaturation, hypotension, any use of vasoactive agents, new arrhythmias), postoperative extrapulmonary complications (sepsis, septic shock, extrapulmonary infection, anastomotic leakage, acute kidney injury), intraoperative fluid balance, impaired wound healing, unplanned admission to an ICU, length of stay in the ICU, length of hospital stay, and all-cause hospital mortality. Definitions for the secondary outcomes are described in the study protocol (Supplement 1).

Statistical Analysis

Assuming a rate of postoperative pulmonary complications of 34% in the low PEEP group and a dropout rate of 2%, an enrollment of 1468 patients would provide 80% power to detect a relative risk reduction of 20% for the incidence of postoperative pulmonary complications at a 2-sided α level of .05.[11,16,23-25]

Discrete variables were summarized as numbers (%), and percentages were calculated according to the number of trial participants for whom data were available. Continuous variables were summarized by either means and SDs or medians and IQRs, according to the observed distribution of the variable.

Statistical analysis was conducted in May 2025. All statistical analyses were performed in the primary analysis population, with patients analyzed according to their assigned treatment groups, excluding those who dropped out before starting treatment. Additionally, a per-protocol analysis was conducted.

The primary and secondary outcomes were assessed using a 2-sided superiority hypothesis test with a significance level of .05 and are presented with a 2-sided 95% CI. In addition to the unadjusted *P* values for secondary outcomes, a Holm-Bonferroni correction to control the family-wide error rate was performed. The effect of high PEEP compared with low PEEP on the incidence of postoperative pulmonary complications was assessed using a mixed-effect generalized linear model with binomial distribution and identity link. Study site was included as a random effect to account for clustering. This model was repeated as a post hoc analysis for the primary and secondary outcomes, with the stratification variables, study site,

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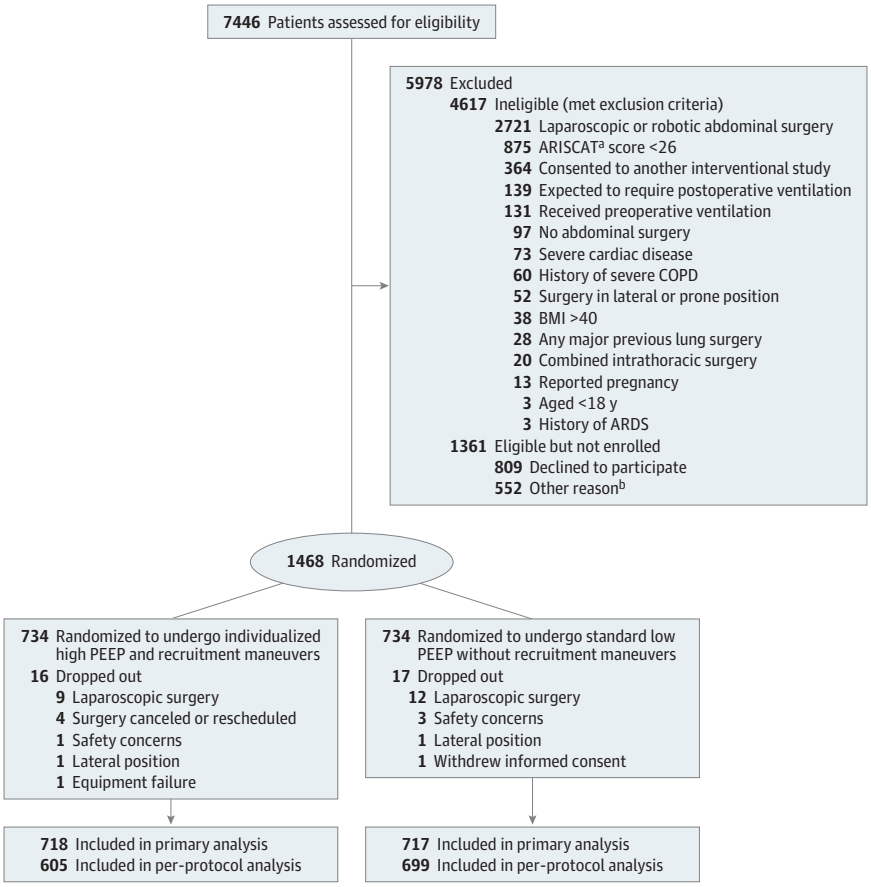
Figure 1. Flow of Patients in the DESIGNATION Trial of Intraoperative Driving Pressure–Guided High Positive End-Expiratory Pressure (PEEP) vs Low PEEP for Postoperative Pulmonary Complications


7446 Patients assessed for eligibility
5978 Excluded
4617 Ineligible (met exclusion criteria)
2721 Laparoscopic or robotic abdominal surgery
875 ARISCAT[a] score <26
364 Consented to another interventional study
139 Expected to require postoperative ventilation
131 Received preoperative ventilation
97 No abdominal surgery
73 Severe cardiac disease
60 History of severe COPD
52 Surgery in lateral or prone position
38 BMI >40
28 Any major previous lung surgery
20 Combined intrathoracic surgery
13 Reported pregnancy
3 Aged <18 y
3 History of ARDS
1361 Eligible but not enrolled
809 Declined to participate
552 Other reason[b]
1468 Randomized
734 Randomized to undergo individualized high PEEP and recruitment maneuvers
16 Dropped out
9 Laparoscopic surgery
4 Surgery canceled or rescheduled
1 Safety concerns
1 Lateral position
1 Equipment failure
734 Randomized to undergo standard low PEEP without recruitment maneuvers
17 Dropped out
12 Laparoscopic surgery
3 Safety concerns
1 Lateral position
1 Withdrew informed consent
718 Included in primary analysis
605 Included in per-protocol analysis
717 Included in primary analysis
699 Included in per-protocol analysis

ARDS indicates acute respiratory distress syndrome; ARISCAT, Assess Respiratory Risk in Surgical Patients in Catalonia; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); COPD, chronic obstructive pulmonary disease; DESIGNATION, Driving Pressure During General Anesthesia for Open Abdominal Surgery.

[a]Scores range from 0 to 123, with higher values indicating greater risk of postoperative pulmonary complications (low risk, <26; intermediate risk, 26-44; high risk, ≥45).

[b]Mainly included logistical issues, language barriers, or no surgeon approval.

and BMI as random effects. Results are reported as absolute differences. To support interpretation, a confidence distribution for the primary outcome using a normal approximation on the estimated absolute difference was calculated.

For other binary outcomes, the effect of high PEEP compared with low PEEP was assessed using the same model we used for the primary outcome. For continuous outcomes, the comparison was made using a mixed-effect median regression model, with sites and BMI category also included as random effects.

For hypothesis-generating purposes, treatment effects on incidence of postoperative pulmonary complications were analyzed according to the following predefined subgroups: (1) age younger than 65 years vs 65 years or older, (2) BMI less than 30 vs 30 or greater, (3) baseline Spo_2 (oxygen saturation measured by pulse oximetry) less than 96% vs 96% or greater, (4) moderate vs high risk for postoperative pulmonary complications according to the ARISCAT risk score (<45 vs ≥45), and (5) planned destination to ICU or high-dependency unit vs ward. Analyses of heterogeneity of effects across subgroups were performed with the use of treatment by subgroup term added to the primary model.

In addition to the analysis described above, the following exploratory analyses were performed: a count analysis, an individual component analysis, a common effect test, and an average relative effect test. There were no missing values for the primary outcome (eTable 1 in Supplement 4). Analyses were performed using R version 4.3.3 (R Foundation).

Results

Patients

From April 1, 2019, through December 20, 2024, 7446 patients were screened at 29 hospitals across 5 countries. After excluding 5978 patients, 1468 were randomized. Of these, 33 (2%) dropped out. A total of 718 patients were randomized to undergo ventilation with high PEEP and 717 to undergo ventilation with low PEEP (**Figure 1**). Baseline demographics were similar between groups; patients were a median (IQR) age of 66 (57-74) years, 52% female, and had a median (IQR) ARISCAT risk score of 41 (34-41) (**Table 1**). The majority of patients (738/1435 [51%]) underwent gynecological or gastrointestinal procedures.

Intervention

Protocol adherence was high and resulted in higher PEEP, peak pressure, plateau pressure, and Spo_2, and a lower driving

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Table 1. Baseline Characteristics of the Included Patients[a]

Characteristic	No. (%)	
	High PEEP (n = 718)	Low PEEP (n = 717)
Age, median (IQR), y	66.0 (57.0-73.0)	65.0 (57.0-73.0)
Age ≥65 y	398 (55.4)	381 (53.1)
Sex		
Female	360 (50.1)	390 (54.4)
Male	358 (49.9)	327 (45.6)
Weight, median (IQR), kg	76.0 (66.0-88.0)	75.0 (64.0-86.0)
BMI, median (IQR)	25.5 (22.9-28.6)	25.2 (22.4-28.4)
BMI ≥30	119 (16.6)	115 (16.0)
ARISCAT score, median (IQR)[b]	41.0 (34.0-41.0)	41.0 (37.0-41.0)
ARISCAT score ≥45	154 (21.4)	152 (21.2)
ASA physical status[c]		
1 - Healthiest	48 (6.7)	54 (7.5)
2	373 (51.9)	411 (57.3)
3	292 (40.7)	244 (34.0)
4 - Least healthy	5 (0.7)	8 (1.1)
Functional status		
Independent	684 (95.3)	696 (97.1)
Partially dependent	33 (4.6)	16 (2.2)
Totally dependent	1 (0.1)	5 (0.7)
Coexisting disorders		
Diabetes	84 (11.7)	85 (11.9)
Coronary artery disease	27 (3.8)	20 (2.8)
COPD	44 (6.1)	36 (5.0)
Smoking status		
Never	321 (44.7)	339 (47.3)
Former[d]	273 (38.0)	272 (37.9)
Current	124 (17.3)	106 (14.8)
Active cancer	514 (71.6)	506 (70.6)
Urgent surgery, No./total No. (%)[e]	19/713 (2.7)	12/713 (1.7)
Procedure[f]		
Gynecology	188 (26.2)	196 (27.3)
Bowel	147 (20.5)	157 (21.9)
Pancreatic	141 (19.6)	123 (17.2)
Urology	113 (15.7)	106 (14.8)
Vascular	62 (8.6)	51 (7.1)
Hepatic	56 (7.8)	63 (8.8)
Gastric	25 (3.5)	25 (3.5)
Biliary	16 (2.2)	15 (2.1)
Other	40 (5.6)	38 (5.3)
Preoperative vital signs, median (IQR)		
Heart rate, bpm	76.0 (67.0-85.0)	77.0 (68.0-87.0)
Systolic blood pressure, mm Hg	134.0 (121.0-146.0)	133.0 (121.0-147.0)
Arterial pressure, mm Hg	96.7 (89.3-105.0)	96.7 (89.3-105.0)
Spo_2, %	97.0 (96.0-98.0)	98.0 (96.0-99.0)
Spo_2 <96%, No./total No. (%)	94/709 (13.3)	86/700 (12.3)
Preoperative chest x-ray	271 (37.7)	276 (38.5)
Atelectasis	10 (1.4)	15 (2.1)
Pleural effusion	8 (1.1)	13 (1.8)
Infiltrates	7 (1.0)	8 (1.1)

(continued)

Table 1. Baseline Characteristics of the Included Patients[a] (continued)

Abbreviations: ARISCAT, Assess Respiratory Risk in Surgical Patients in Catalonia; ASA, American Society of Anesthesiologists; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); COPD, chronic obstructive pulmonary disease; PEEP, positive end-expiratory pressure; Spo_2, oxygen saturation measured by pulse oximetry.

[a] Denominators are reported only when missing data are present; if no denominator is shown, the variable is complete.

[b] Scores range from 0 to 123, with higher values indicating greater risk of postoperative pulmonary complications (low risk, <26; intermediate risk, 26-44; high risk, ≥45).

[c] Higher classes indicate greater preoperative comorbidity and perioperative risk.

[d] Cessation of more than 3 months.

[e] Surgery that could not be delayed for more than 24 hours.

[f] Patients could have more than 1 type of procedure.

pressure in the high PEEP group compared with the low PEEP group (**Table 2**). These differences remained throughout the entire procedure (eFigures 2 and 3 in Supplement 4). Preapproved rescue strategies for hypoxemia were used more frequently in the low PEEP group (eTable 2 in Supplement 4). PEEP was adjusted for predefined clinical reasons in 61 patients (8.5%) in the intervention group vs 12 patients (1.7%) in the control group. Other intraoperative characteristics, including the use of epidural anesthesia, were not different between both groups (eTables 3 and 4 in Supplement 4).

Outcomes

The incidence of the composite measure of postoperative pulmonary complications in the first 5 postoperative days was not different between patients in the high PEEP group (19.8%) compared with patients in the low PEEP group (17.4%) (absolute difference, 2.5% [95% CI, −1.5% to 6.4%]; P = .23) (**Figure 2** and **Table 3**). The confidence in a benefit with the intervention was 11.7% (eFigure 4 in Supplement 4). The analysis regarding the 6 prespecified subgroups suggested benefit of low PEEP in patients who were planned to go to an ICU or high-dependency unit postoperatively (Figure 2) (eFigure 5 in Supplement 4). The per-protocol analysis did not change the findings (eTable 5 in Supplement 4).

Of the 16 secondary end points, 13 were not different (Table 3). Hypotension occurred more often, and vasopressors were more frequently used in the high PEEP group, while desaturations occurred more often in the low PEEP group. The difference in incidence of hypotension and use of vasopressors remained statistically significant after correction for multiple testing (eTable 6 in Supplement 4).

Sensitivity and Post Hoc Analyses

Of the 4 sensitivity analyses, the common effect and average relative effect generalized estimating equations suggested

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Table 2. Ventilation Characteristics[a]

Characteristic	Median (IQR)		Absolute difference, % (95% CI)
	High PEEP (n = 718)	Low PEEP (n = 717)	
Patients with recruitment maneuvers, No. (%)	711 (99.0)	1 (0.1)	98.7 (97.9 to 99.6)
No. of recruitment maneuvers	3 (3 to 3)	0	3.0 (3.0 to 3.0)
No nadir identified during PEEP titration, No. (%)	71 (10.0)	NA	NA
Lowest ΔP during PEEP titration, cm H_2O	7 (6 to 8)	NA	NA
Tidal volume, mL/kg PBW			
After intubation[b]	8.0 (7.8 to 8.0)	8.0 (7.8 to 8.0)	0
After first hour[c]	7.9 (7.8 to 8.0)	7.9 (7.8 to 8.0)	0
Final measurement[d]	8.0 (7.8 to 8.0)	8.0 (7.8 to 8.0)	0
PEEP, cm H_2O			
After intubation	5 (5 to 5)	5 (5 to 5)	0
After first hour	10 (10 to 12)	5 (5 to 5)	5.0 (5.0 to 5.0)
Final measurement	10 (8 to 12)	5 (5 to 5)	5.0 (5.0 to 5.0)
Peak pressure, cm H_2O			
After intubation	18 (16 to 21)	18 (16 to 20)	0 (−1.1 to 1.1)
After first hour	23 (20 to 25)	18 (16 to 20)	5.0 (4.2 to 5.8)
Final measurement	22 (20 to 25)	18 (16 to 20)	4.0 (3.0 to 5.0)
Plateau pressure, cm H_2O			
After intubation	15 (13 to 17)	14 (13 to 16)	1.0 (0.5 to 1.5)
After first hour	19 (17 to 21)	15 (13 to 17)	4.0 (3.8 to 4.2)
Final measurement	19 (17 to 21)	15 (13 to 17)	4.0 (3.8 to 4.2)
Driving pressure, cm H_2O			
After intubation	10 (8 to 12)	9 (8 to 11)	1.0 (0.1 to 1.9)
After first hour	8 (7 to 10)	10 (8 to 12)	−2.0 (−2.4 to −1.6)
Final measurement	8 (7 to 10)	10 (8 to 12)	−2.0 (−2.4 to −1.6)
Respiratory rate, breaths/min			
After intubation	13 (12 to 15)	12 (12 to 15)	1.0 (−0.3 to 2.3)
After first hour	11 (10 to 12)	11 (10 to 12)	0 (−0.9 to 0.9)
Final measurement	12 (10 to 14)	12 (10 to 13)	0 (−0.1 to 0.1)
F_{IO_2}			
After intubation	0.40 (0.40 to 0.52)	0.40 (0.40 to 0.50)	0
After first hour	0.40 (0.40 to 0.40)	0.40 (0.40 to 0.42)	0
Final measurement	0.40 (0.40 to 0.40)	0.40 (0.40 to 0.44)	0
Spo_2, %			
After intubation	100 (99 to 100)	100 (99 to 100)	0
After first hour	100 (98 to 100)	99 (98 to 100)	1.0 (0.5 to 1.5)
Final measurement	100 (99 to 100)	99 (98 to 100)	1.0 (0.4 to 1.6)
$etCO_2$, mm Hg			
After intubation	34.0 (31.5 to 36.8)	34.0 (31.5 to 36.0)	0 (−0.6 to 0.6)
After first hour	34.5 (32.3 to 36.0)	34.0 (32.3 to 36.0)	0.5 (−0.1 to 1.1)
Final measurement	36.0 (33.8 to 37.5)	36.0 (33.8 to 37.5)	0 (−0.9 to 0.9)

Abbreviations: ΔP, driving pressure; $etCO_2$, end-tidal carbon dioxide; F_{IO_2}, fraction of inspired oxygen; NA, not applicable; PBW, predicted body weight; PEEP, positive end-expiratory pressure; Spo_2, oxygen saturation measured by pulse oximetry.

[a] Denominators are reported only when missing data are present; if no denominator is shown, the variable is complete.

[b] First stable reading after intubation.

[c] Measurement taken 1 hour after the first reading.

[d] Final intraoperative measurement before extubation.

benefit of low PEEP (eTable 5 in Supplement 4). The post hoc analysis did not change the results.

Discussion

Among adult patients undergoing open abdominal surgery at increased risk for postoperative pulmonary complications, ventilation with an intraoperative ventilation strategy with an individualized, driving pressure–guided, high PEEP and recruitment maneuvers did not reduce postoperative pulmonary complications compared with ventilation with standard low PEEP without recruitment maneuvers. During the intraoperative period, hypotension and use of vasopressors were more frequent in patients randomized to the high PEEP group, whereas desaturations occurred more often in the low PEEP group.

The intervention strategy—ventilation with an individualized high level of PEEP combined with recruitment maneuvers—was selected to create contrast in PEEP between the groups. In the intervention group, the study investigators

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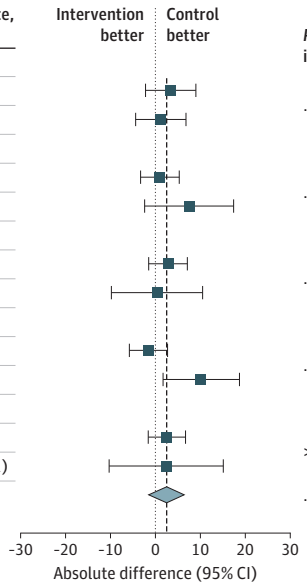
Figure 2. Incidence of Postoperative Pulmonary Complications in Prespecified Subgroups

Subgroup	No./total No. (%)		Absolute difference, % (95% CI)	P value for interaction
	High PEEP	Low PEEP		
Age, y				
<65	57/320 (17.8)	48/336 (14.3)	3.4 (-2.2 to 9.0)	.60
≥65	85/398 (21.4)	77/381 (20.2)	1.2 (-4.4 to 6.8)	
ARISCAT				
Moderate risk	94/564 (16.7)	89/565 (15.8)	1.0 (-3.3 to 5.3)	.18
High risk	48/154 (31.2)	36/152 (23.7)	7.5 (-2.4 to 17.4)	
BMI				
<30	118/599 (19.7)	102/602 (16.9)	2.8 (-1.5 to 7.1)	.71
≥30	24/119 (20.2)	23/115 (20.0)	0.4 (-9.8 to 10.5)	
Planned ICU or HDU admission				
No	67/497 (13.5)	77/514 (15.0)	-1.5 (-5.8 to 2.7)	.007
Yes	75/221 (33.9)	48/203 (23.6)	10.1 (1.7 to 18.7)	
Spo_2, %				
≥96	114/615 (18.5)	99/614 (16.1)	2.5 (-1.6 to 6.7)	>.99
<96	25/94 (26.6)	21/86 (24.4)	2.5 (-10.3 to 15.1)	
Overall	142/718 (19.8)	125/717 (17.4)	2.5 (-1.5 to 6.4)	.23



ARISCAT indicates Assess Respiratory Risk in Surgical Patients in Catalonia; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HDU, high-dependency unit; ICU, intensive care unit; PEEP, positive end-expiratory pressure; Spo_2, oxygen saturation measured by pulse oximetry.

The diamond indicates the absolute difference and the dashed line, the 95% CI.

wanted to prevent inducing higher levels of driving pressure, aiming to balance alveolar recruitment and avoidance of overdistension.[13] The intervention followed a previously reported PEEP titration strategy.[14] In the control group, standard PEEP without recruitment maneuvers was used to reflect routine clinical practice.[1] This resulted in higher PEEP and lower driving pressure in the high PEEP group, consistent with findings from other studies in open abdominal surgery.[14,16,17,26] The contrast in PEEP between the groups and the reduction in driving pressure in the intervention group confirmed that the intervention achieved its physiologic target. PEEP requirements in the high PEEP group varied widely, also in line with previous investigations.[14] These findings underscore how individualized PEEP can enhance alveolar recruitment while limiting overdistension.

The findings of this study contrast with those of an earlier randomized clinical trial in patients undergoing major abdominal surgery, which tested a similar intervention using driving pressure-guided individualized high PEEP, demonstrating a reduction in postoperative pulmonary complications.[26] However, this trial included substantially fewer patients, thereby limiting precision of the results obtained. Another study suggested benefit from a compliance-guided, individualized high PEEP strategy,[16] which closely resembled a driving pressure-guided approach. Notably, the observed benefit in that study was confined to a combined intraoperative and postoperative individualized strategy consisting of continuous positive airway pressure. It remains uncertain whether the benefit resulted from the intraoperative intervention, the postoperative component, or both. Moreover, that study included both open and laparoscopic abdominal procedures. Study findings are consistent with a 2025 randomized clinical trial that evaluated individualized compliance-guided high PEEP as part of a perioperative bundle aimed at reducing postoperative pulmonary complications.[17] Taken together, current evidence suggests that future research should prioritize perioperative lung-protective strategies because intraoperative optimization alone may be insufficient to improve clinical outcomes.

The high PEEP strategy was associated with increased incidence of hypotension and greater use of vasopressors, a finding similarly reported in previous randomized clinical trials comparing high vs low PEEP.[11,12,17] Given the low probability of benefit with regard to postoperative pulmonary complications alongside the increased occurrence of hemodynamic complications, one could argue that intraoperative high PEEP may be more appropriate as a rescue intervention rather than a routine ventilation strategy.

This randomized clinical trial has several strengths. First, the study had a pragmatic design, randomization led to well-balanced patient cohorts, and it was conducted in both teaching and nonteaching hospitals in 5 countries, making the results generalizable. Second, ventilation in the control group reflected current clinical practice. Third, the intervention proved to be highly feasible, with excellent adherence across all participating centers.[20] Fourth, bias was minimized by using concealed randomization, blinding of outcome assessors, an intention-to-treat analysis, and no loss to follow-up. Fifth, the statistical analysis plan, published before closing the database, was strictly followed, enhancing the validity and reliability of the findings. Sixth, all centers were encouraged to adhere to the ERAS guidelines.

Limitations

This study has limitations. First, the composite primary outcome included postoperative pulmonary complications of varying severity. Interpreting a composite outcome is challenging because components rarely meet the ideal criteria of having comparable clinical importance, frequency, and treatment effects. However, the effect of the intervention on individual components in several sensitivity analyses confirmed the main

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Table 3. Primary and Secondary Outcomes

Outcome	No./total No. (%)		Absolute difference, % (95% CI)	*P* value[a]
	High PEEP (n = 718)	Low PEEP (n = 717)		
Primary outcome				
Postoperative pulmonary complications	142/718 (19.8)	125/717 (17.4)	2.5 (−1.5 to 6.4)	.23
Severe respiratory failure	13/718 (1.8)	10/717 (1.4)	0.4 (−0.9 to 1.7)	.53
Bronchospasm	1/718 (0.1)	1/717 (0.1)	0 (−0.4 to 0.4)	>.99
Suspected pulmonary infection	24/718 (3.3)	14/717 (2.0)	1.4 (−0.3 to 3.0)	.10
Pulmonary infiltrates	21/718 (2.9)	16/717 (2.2)	0.7 (−1.0 to 2.3)	.42
Aspiration pneumonitis	2/718 (0.3)	1/717 (0.1)	0.1 (−0.3 to 0.6)	.59
Atelectasis	87/718 (12.1)	75/717 (10.5)	1.7 (−1.5 to 5.0)	.30
Acute respiratory distress syndrome	4/718 (0.6)	2/717 (0.3)	0.3 (−0.4 to 0.9)	.42
Pleural effusion	87/718 (12.1)	77/717 (10.7)	1.5 (−1.7 to 4.8)	.36
Cardiopulmonary edema	17/718 (2.4)	15/717 (2.1)	0.3 (−1.2 to 1.8)	.72
Pneumothorax	10/718 (1.4)	8/717 (1.1)	0.3 (−0.9 to 1.4)	.64
Secondary outcomes				
Mild respiratory failure	112/718 (15.6)	120/717 (16.7)	−1.1 (−4.8 to 2.6)	.56
Intraoperative complications	424/709 (59.8)	344/707 (48.7)	11.4 (7.0 to 15.7)	<.001
Desaturation	6/716 (0.8)	20/716 (2.8)	−2.0 (−3.3 to −0.6)	.005
Hypotension	382/708 (54.0)	317/704 (45.0)	9.0 (4.7 to 13.4)	<.001
Use of vasoactive agents	224/700 (32.0)	130/690 (18.8)	13.2 (9.0 to 17.4)	<.001
New arrhythmias	8/694 (1.2)	4/681 (0.6)	0.6 (−0.4 to 1.5)	.26
Postoperative extrapulmonary complications	73/718 (10.2)	68/717 (9.5)	0.7 (−2.3 to 3.7)	.64
Sepsis	10/718 (1.4)	9/717 (1.3)	0.1 (−1.0 to 1.3)	.83
Septic shock	6/718 (0.8)	9/717 (1.3)	−0.4 (−1.5 to 0.6)	.44
Extrapulmonary infection	19/718 (2.6)	24/717 (3.3)	−0.6 (−2.4 to 1.1)	.47
Anastomotic leakage	15/718 (2.1)	16/717 (2.2)	−0.1 (−1.6 to 1.4)	.86
Acute kidney injury	48/718 (6.7)	38/717 (5.3)	1.4 (−1.0 to 3.8)	.26
Intraoperative fluid balance, median (IQR)	1380 (700 to 2329)	1259 (600 to 2200)	120.2 (−64.8 to 305.2)	.20
Impaired wound healing	23/718 (3.2)	27/717 (3.8)	−0.6 (−2.5 to 1.3)	.54
Unplanned admission to ICU	9/718 (1.3)	18/717 (2.5)	−1.3 (−2.7 to 0.1)	.07
ICU length of stay, median (IQR), d	0 (0 to 1.0)	0 (0 to 1.0)	0 (−0.1 to 0.1)	>.99
Hospital length of stay, median (IQR), d	6.0 (5.0 to 10.0)	6.0 (5.0 to 10.0)	0 (−0.4 to 0.4)	>.99
All-cause hospital mortality	25/698 (3.6)	23/703 (3.3)	0.3 (−1.6 to 2.2)	.75

Abbreviations: ICU, intensive care unit; PEEP, positive end-expiratory pressure.

[a] *P* values computed using a mixed-effect generalized linear model with binomial distribution and identity link, with study site included as a random effect.

findings. Second, the incidence of postoperative pulmonary complications was lower than expected, which reduced the precision of the estimated effect. Nevertheless, the likelihood of support for the initial hypothesis remained low, and the CI excluded a clinically relevant benefit. Third, patients planned for minimally invasive surgery were excluded from participation. Therefore, the findings of this study cannot be generalized to these patients. Fourth, neuromuscular monitoring and reversal were not protocolized, which could have influenced the results. Fifth, although the subgroup analyses were informative to illustrate consistency of the treatment effect across clinically relevant populations, the sample size was small and therefore gave imprecise results.

Conclusions

Among patients undergoing open abdominal surgery at increased risk for postoperative pulmonary complications, an intraoperative strategy of individualized driving pressure–guided high PEEP with recruitment maneuvers, compared with a strategy of standard low PEEP without recruitment maneuvers, did not reduce postoperative pulmonary complications.

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ARTICLE INFORMATION

Accepted for Publication: November 10, 2025.

Published Online: December 3, 2025. doi:10.1001/jama.2025.23373

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Obtained funding: Gama de Abreu, Hollmann, Schultz, Serpa Neto.
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Conflict of Interest Disclosures: Dr Gama de Abreu reported receiving personal fees from Ambu outside the submitted work. Dr Hol reported receiving grants from ZonMw during the conduct of the study. Dr Hollmann reported receiving grants from ZonMw during the conduct of the study and outside the submitted work; and serving as executive section editor of pharmacology for *Anesthesia & Analgesia*, section editor of anesthesiology for *Journal of Clinical Medicine*, and editor of *Frontiers in Physiology*. Dr van Meenen reported receiving grants from ZonMw and European Society of Anaesthesiology and Intensive Care during the conduct of the study. Dr Serpa Neto reported receiving personal fees from Hamilton Medical outside the submitted work. No other disclosures were reported.

Funding/Support: This study was supported by a research grant from ZonMw (852001922).

Role of the Funder/Sponsor: ZonMw had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Group Information: The members of the DESIGNATION–Investigators are listed in Supplement 5.

Data Sharing Statement: See Supplement 6.

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